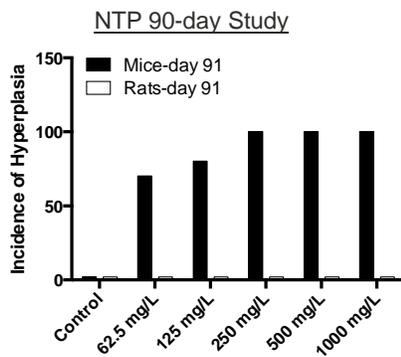


# Science Question 3: Susceptibility of Mice to Gastrointestinal Toxicity

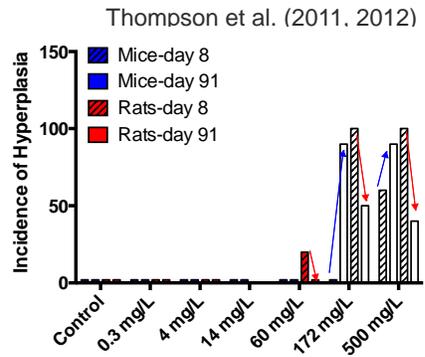
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ToxStrategies, Inc.  
Supported by ACC  
June 25, 2014



## Incidence of Intestinal Hyperplasia in 90-Day Studies



Implication: mice are more susceptible than rats



Implications: mice and rats are qualitatively similar; effects in rats might have been subsiding...



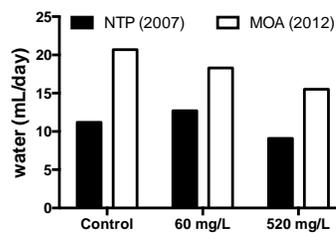
## 90-Day Rat Study Report Concluded:

### Southern Research:

"The microscopic lesions...were consistent with the type of **non-neoplastic lesions** that were observed in previous studies in... rats (histiocytic cellular infiltration) or mice (histiocytic cellular infiltration, diffuse epithelial hyperplasia) for 2 years...**In the current rat study, the intestinal lesions were more similar to lesions observed in the previous mouse study than to the previous rat study.** The reason for this discrepancy...is unknown."



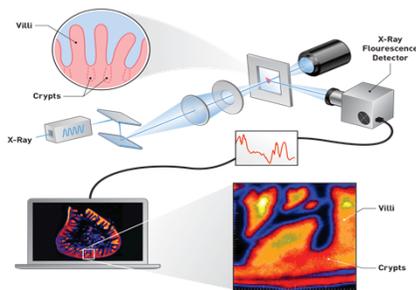
- Blunting & thickening of villi
- Histiocytic cells in lamina propria of villus tips
- Elongation of crypts (regenerative hyperplasia)



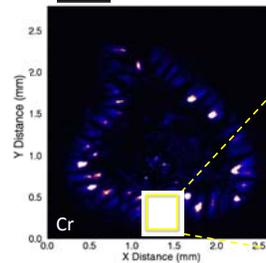
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## Cr is Limited to Intestinal Villi in Both Species (Proliferation is Therefore Secondary to Villous Toxicity)

### X-ray Fluorescence (Spectro)microscopy



### Mice



### Rats

